Attorney Docket No.: 6169.200-US PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Liselotte Bjerre Knudsen

Application No.: 09/800,541 Group Art Unit: 1647

Filed: March 7, 2001 Examiner: Romeo, David S.

Confirmation No. 4130

For: Lowering Serum Lipids

APPEAL BRIEF

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Commissioner for Patents
P.O. Box 1450
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Dear Sir:

This appellant's brief under 37 C.F.R. §41.37 is submitted in triplicate in the appeal of the final Office Action transmitted by facsimile on January 22, 2004.

I. Real Party in Interest

The real party in interest is Novo Nordisk A/S, the assignee of this application by assignments recorded on August 6, 2001, at Reel 012062, Frame 0533 and on March 12, 2002, at Reel 012699, Frame 0671.

II. Related Appeals and Interferences

There are no other appeals or interferences which bear on the present appeal.

III. Status of Claims

Claims 26-29 and 36-72 are pending, rejected, and appealed. Claims 1-25 and 30-35 were cancelled.

IV. Status of Amendments

The final Office Action was transmitted on January 22, 2004. An Amendment and Response pursuant to 37 C.F.R. 1.116, a Notice of Appeal, and a Petition and Fee for Extension of Time were mailed on June 1, 2004. An Advisory Action was mailed on July 29, 2004, entering the Amendment and Response. However, claims 26-29 and 36-72 remained rejected.

V. Summary of Claimed Subject Matter

The presently claimed invention is directed to methods for (1) lowering the levels of one or more serum lipids, (2) reducing the serum LDL:HDL ratio, or (3) reducing the serum level of lipoprotein A (lp(A)) and/or apolipoprotein A (apo(A)) in a patient in need of each, respectively. The methods are performed by respectively administering (1) a lipid-lowering effective amount, (2) an amount effective to reduce the LDL:HDL ratio, or (3) an amount effective to reduce the serum level of lipoprotein A (lp(A)) and/or apolipoprotein A (apo(A)) of GLP-1 (7-37), GLP-1 (7-36) amide, exendin-3, exendin-4, or an analogue or derivative of the foregoing. This agent is respectively administered to (1) a patient in need of having one or more serum levels lowered, (2) a patient in need of reduction of the LDL:HDL ratio, or (3) a patient in need of reduction of the serum level of lipoprotein A (lp(A)) and/or apolipoprotein A (apo(A)). This means that the present claims each require administering the agent with the intent to achieve the stated objective, *i.e.*, treatment of the specified condition. *See Jansen v. Rexall Sundown, Inc.*, 342 F.3d 1329, 1333, 68 U.S.P.Q.2d 1154, 1158 (Fed. Cir. 2003).

VI. Grounds of Rejection to be Reviewed on Appeal

1. Whether the Examiner erred in rejecting claims 26-29, 36-42, 44-46, 48, 49, 51, 52, 54-56, 58, 59, 61, 62, 64-66, 68, 69, 71, and 72 under 35 U.S.C. 102(b) as anticipated by Eng, U.S. Patent No. 5,424,286, in view of Raufman et al., J. Biol. Chem., 267:30, 21432-21437 (Oct. 1992) and in view of Howard, Cur. Op. in Lipidology, 5:216-220 (1984).

2. Whether the Examiner erred in rejecting claims 26, 27, 29, 36, 37, 39, 40, 42-46, 48, 49, 52, 54-56, 58, 59, 62-66, 68, 69, and 72 under 35 U.S.C. 102(b) as anticipated by Efendic et al., U.S. Patent No. 5,631,224 in view of Howard, Cur. Op. in Lipidology, 5:216-220 (1984).

3. Whether the Examiner erred in rejecting claims 26-29 and 36-72 under 35 U.S.C. 112, first paragraph as lacking enablement for a method of lowering one or more serum lipids, reducing the serum LDL:HDL ration, and reducing the serum level of lp(A) or apo(A).

4. Whether the Examiner erred in rejecting claims 26-29 and 36-72 under 35 U.S.C. 112, first paragraph as lacking a written description of the full scope of the pending claims, i.e., lowering one or more serum lipids, reducing the serum LDL:HDL ratio, and reducing the serum level of lp(A) or apo(A).

5. Whether the Examiner erred in rejecting claims 26, 27, 29, 36, 37, 39, 40, 42, 44-49, 52, 54-59, 62, 64-69, and 72 under 35 U.S.C. 112, first paragraph as lacking a written description of the

full scope of the pending claims, i.e., "'analogue' or 'derivative,' 'derivative of an analogue,' or 'exendin-4 analogue'". Final Office Action, p. 7.

6. Whether the Examiner erred in rejecting claims 26-29, 36-42, 44-50, 52, 54-60, 62, 64-70, and 72 under the judicially created doctrine of obviousness-type double patenting over claims 39 and 40 of U.S. Patent No. 6,268,343 in view of Howard, Cur. Op. in Lipidology, 5:216-220 (1984) and Efendic et al., U.S. Patent No. 5,631,224.

7. Whether the Examiner erred in rejecting claims 26-29, 36-42, 44-50, 52, 54-60, 62, 64-70, and 72 under the judicially created doctrine of obviousness-type double patenting over claims 19 and 20 of U.S. Patent No. 6,458,924 in view of Howard, Cur. Op. in Lipidology, 5:216-220 (1984) and Efendic et al., U.S. Patent No. 5,631,224.

8. Whether the Examiner erred in rejecting claims 44-49, 52, 54-59, 62, 64-69, and 72 under 35 U.S.C. 112, second paragraph as indefinite "because they recite the term 'analogue' or 'derivative,' 'derivative of an analogue,' or 'exendin-4 analogue'". Final Office Action, p. 10.

9. Whether the Examiner erred in rejecting claims 45, 49, 55, 59, 65, and 69 under 35 U.S.C. 112, second paragraph as indefinite "because it is unclear if the analog is GLP-1(7-37) with a single amino acid substitution or some wholly undefined compound comprising an amino acid that is

different from an amino acid in the corresponding position of GLP-1(7-37)." Final Office Action. p. 11.

VII. Argument

A. Grounds of Rejection 1 and 2

The Examiner improperly rejected claims 26-29, 36-42, 44-46, 48, 49, 51, 52, 54-56, 58, 59, 61, 62, 64-66, 68, 69, 71, and 72 under 35 U.S.C. 102(b) as anticipated by Eng, U.S. Patent No. 5,424,286, in view of Raufman et al., J. Biol. Chem., 267:30, 21432-21437 (Oct. 1992) and in view of Howard, Cur. Op. in Lipidology, 5:216-220 (1984). The Examiner also improperly rejected claims 26, 27, 29, 36, 37, 39, 40, 42-46, 48, 49, 52, 54-56, 58, 59, 62-66, 68, 69, and 72 under 35 U.S.C. 102(b) as anticipated by Efendic et al., U.S. Patent No. 5,631,224, in view of Howard. The rejections are improper because the Examiner has misunderstood what is claimed. The prior art does not disclose what is claimed.

The first step in any invalidity analysis is claim construction. The meaning of the claim is ascertained. *Teleflex, Inc. v. Ficosa N. Am. Corp.,* 299 F.3d 1313, 1323-33, 63 U.S.P.Q.2d 1374, 1379 (Fed. Cir. 2002)*; Bristol-Myers Squibb Co. v. Ben Venue Labs., Inc.,* 246 F.3d 1368, 1375, 58 U.S.P.Q.2d 1508, 1513 (Fed. Cir. 2001*); Rockwell Int'l Corp. v. United States,* 147 F.3d 1358, 1362, 47 U.S.P.Q.2d 1027, 1029 (Fed. Cir. 1998). *See also Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 976, 979, 34 U.S.P.Q.2d 1321, 1327, 1329 (Fed. Cir. 1995).

Claim interpretation is a question of law, *Markman*, 517 U.S. 370, 372, 116 S. Ct. 1384, 1387, 38 U.S.P.Q.2d 1461, 1463 (1996), and in that sense, is no different than the interpretation of written legal documents in general. *Markman*, 52 F.3d at 978-79, 34 U.S.P.Q.2d at 1328-1329. *See*

also Hormone Research Found. Inc. v. Genentech, Inc., 904 F.2d 1558, 1562, 15 U.S.P.Q.2d 1039, 1042-1043 (Fed. Cir. 1990), *cert. dismissed*, 499 U.S. 955 (1991). Meaning must be given to every element of the claim. *See Union Water-Meter Co. v. Desper Products, Inc.*, 101 U.S. 332, 337 (1879).

When construing a claim, one should look first to the intrinsic evidence of record, i.e., the patent itself including the claims, the specification, and the prosecution history. *CVI/Beta Ventures, Inc. v. Tura LP*, 112 F.3d 1146, 1152, 42 U.S.P.Q.2d 1577, 1582 (Fed. Cir. 1997), *cert. denied*, 522 U.S. 1109 (1998). This evidence "is the most significant source of the legally operative meaning of disputed claim language." *Vitronics Corp. v. Conceptronics, Inc.*, 90 F.3d 1576, 1582, 39 U.S.P.Q.2d 1573, 1576 (Fed. Cir. 1996).

The words of the claim are given their ordinary meaning to one skilled in the art unless it appears from the application and file history that the words were used differently by the inventors. *Id.*, 90 F.3d at 1582, , 39 U.S.P.Q.2d at 1573; *Rexnord Corp. v. Laitram Corp.*, 274 F.3d 1336, 1342 60 U.S.P.Q.2d 1851, 1854 (Fed.Cir. 2001); *Transmatic, Inc. v. Gulton Indus., Inc.*, 53 F.3d 1270, 1277, 35 U.S.P.Q.2d 1035, 1040 (Fed. Cir. 1995); *Envirotech Corp. v. Al George, Inc.*, 730 F.2d 753, 759, 221 U.S.P.Q. 473, 477 (Fed. Cir. 1994). Common words, unless the context suggests otherwise, should be accorded their ordinary meaning. *Desper Products, Inc. v. QSound Labs, Inc.*, 157 F.3d 1325, 1336, 48 U.S.P.Q.2d 1088, 1097 (Fed. Cir. 1998). *See also Hockerson-Halberstadt, Inc. v. Avia Group Int'l, Inc.*, 222 F.3d 951, 955, 55 U.S.P.Q.2d 1487, 1490 (Fed. Cir. 2000) (The claim term's ordinary and accustomed meaning initially serves as a default meaning, unless the patentee or applicant ascribes a different or modified meaning to the term).

A technical term used in a patent application is interpreted as having the meaning that it would be given by persons experienced in the field of the invention, unless it is apparent from the application and the prosecution history that the invention used the term with a different meaning. *Vitronics*, 90 F.3d at 1582, 39 U.S.P.Q.2d at 1576 (quoting *Hoechst Celanese v. BP Chems. Ltd.*, 78 F.3d 1575, 1578, 38 U.S.P.Q.2d 1126 (Fed. Cir. 1996), *cert denied*, 519 U.S. 911 (1996)). A court may rely upon extrinsic evidence to educate itself about the underlying technology, but cannot use extrinsic evidence to arrive at a claim construction that is inconsistent with a construction that is mandated by the intrinsic evidence. *Key Pharmaceuticals v. Hercon Labs Corp.*, 161 F.3d 709, 716, 48 U.S.P.Q.2d 1911, 1917 (Fed. Cir. 1998).

Once the proper meaning of a term used in a claim has been discerned, that term must have the same meaning for all claims in which it appears. *Southwall Techs. Inc. v. Cardinal IG Co.*, 54 F.3d 1570, 1579, 34 U.S.P.Q.2d 1673, 1679 (Fed. Cir. 1995), *cert. denied*, 516 U.S. 987 (1995) (a claim term "cannot be interpreted differently in different claims").

Ordinarily, where the complete invention is described in the claim body and the preamble merely states a purpose or intended use for the invention, the preamble is not a claim limitation. *Rowe v. Dror*, 112 F.3d 473, 478-79, 42 U.S.P.Q.2d 1550, 1553 (Fed. Cir. 1997). However, if the preamble of a claim is necessary to give meaning to the claim and to define properly the invention, the preamble is a claim limitation. *DeGeorge v. Bernier*, 768 F.2d 1318, 1322 n.3, 226 U.S.P.Q. 758, 761 n.3 (Fed. Cir. 1985).

Every presently appealed claim includes a preamble that, *inter alia*, states the specific purpose of the claim. Independent claim 26 and its dependent claims 27-36 and 43-52 are methods

"for lowering levels of one or more serum lipids in a patient." Independent claim 37 and its dependent claims 38, 39, and 51-62 27-36 and 43-52 are methods "for reducing the serum LDL:HDL ratio in a patient." Independent claim 40 and its dependent claims 41, 42, and 63-72 are methods "for reducing the serum level of lipoprotein A (lp(A)) and/or apolipoprotein A (apo(A))."

However, that is not the only function of the preambles of the presently appealed claims. These preambles are also necessary to give meaning to the claims and provide positive limitations to the claims. Every appealed claim's preamble is a limitation that requires "that the method be practiced with the intent to achieve the stated objective." *Jansen,* 342 F.3d at 1333, 68 U.S.P.Q.2d at 1158. Independent claim 26 and its dependent claims 27-36 and 43-52 call for administration to "a patient in need of having one or more serum levels lowered." Independent claim 37 and its dependent claims 38, 39, and 51-62 27-36 and 43-52 call for administration to "a patient in need of reduction of said LDL:HDL ratio." Independent claim 40 and its dependent claims 41, 42, and 63-72 call for administration to "a patient in need of reduction of the serum level of lipoprotein A (lp(A))." These latter terms ("a patient in need of ...) give life and meaning to the statements of purpose in the respective preambles. *Jansen*, 342 F.3d at 1333, 68 U.S.P.Q.2d at 1158, citing *Kropa v. Robie*, 187 F.2d 150, 152, 88 U.S.P.Q.2d 478, 480 (C.C.P.A. 1951). Accordingly, the preambles are statements of the intentional purposes for which the methods must be performed. They are not merely statements of affect that may or may not be desired or appreciated. Rather, the preambles are limitations of the claims, and the claims require intent.

An invention that is patentable in the United States must be, *inter alia*, novel. An invention is not novel and is anticipated under 35 U.S.C. §102(b), if more than one year before the filing date

of the application, the invention was: (a) patented or described in a printed publication in the United States or in a foreign country; or (b) was in public use or on sale in the United States. The test is whether, "each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference" or prior public use. *Constant v. Advanced Micro-Devices, Inc.*, 848 F.2d 1560, 1570, 7 U.S.P.Q.2d 1057, 1064 (Fed. Cir. 1988), *cert. denied*, 488 U.S. 892 (1988); *Minnesota Mining and Mfg. Co. v. Johnson & Johnson Orthopaedics, Inc.* 976 F.2d 1559, 1565, 24 U.S.P.Q.2d 1321, 1326 (Fed. Cir. 1992); *In re Schreiber,* 128 F.3d 1473, 1477, 44 U.S.P.Q.2d 1429, 1431 (Fed. Cir. 1997), *see also Schering Corp. v. Geneva Pharm., Inc.*, 339 F.3d 1373, 1377, 67 U.S.P.Q.2d 1664, 1668 (Fed. Cir. 2003).

Anticipation is a question of fact, including whether or not an element is inherent in the prior art. *Atlas Powder Co. v. IRECO Inc.*, 190 F.3d 1342, 1346, 51 U.S.P.Q.2d 1943, 1945 (Fed. Cir. 1999). A characteristic is inherent in a reference when evidence makes it clear that the missing descriptive matter is necessarily present in the reference and that it would be so recognized by persons of ordinary skill. *Schering Corp. v. Geneva Pharm. Inc.*, 339 F.3d 1373, 1377, 67 U.S.P.Q.2d 1664, 1668 (Fed. Cir. 2003), *Continental Can Co. v. Monsanto Co.,* 948 F.2d 1264, 1268, 20 U.S.P.Q.2d 1746, 1749 (Fed. Cir. 1991). One simple test to determine whether a reference or use is anticipatory is to determine whether that reference or use would literally infringe the claim at issue, because "[t]hat which would *literally* infringe if later in time anticipates if earlier than the date of invention." *Lewmar Marine, Inc. v. Barient, Inc.* 827 F.2d 744, 747, 3 U.S.P.Q.2d 1766, 1767-1768 (Fed. Cir. 1987), *cert. denied*, 484 U.S. 1007 (1988).

The prior art relied upon by the Examiner in the present appeal does not expressly or inherently disclose the administration of GLP-1 (7-37), GLP-1 (7-36) amide, exendin-3, exendin-4, or an analogue or derivative of the foregoing with the intent of (1) lowering the levels of one or more serum lipids, (2) reducing the serum LDL:HDL ratio, or (3) reducing the serum level of lipoprotein A (lp(A)) and/or apolipoprotein A (apo(A)) in a patient in need of each, respectively.

The first primary reference relied upon by the Examiner is by Eng, U.S. Patent No. 5,424,286. However, Eng discloses only the use of exendin-3 or exendin-4 with the intent of treating of diabetes mellitus and the intent of preventing hyperglycemia. col. 2, ll. 36-40. There is no disclosure of administering anything with the intent of (1) lowering the levels of one or more serum lipids, (2) reducing the serum LDL:HDL ratio, or (3) reducing the serum level of lipoprotein A (lp(A)) and/or apolipoprotein A (apo(A)) in a patient in need of each, as presently claimed. Consequently, Eng cannot anticipate pending claims 26-29, 36-42, 44-46, 48, 49, 51, 52, 54-56, 58, 59, 61, 62, 64-66, 68, 69, 71, and 72.

Furthermore, Eng states that the action of exendins in treating diabetes mellitus and in preventing hyperglycemia is dependent on blood glucose concentration. col. 2, ll. 51-55. This means that the effects of exendins on diabetes mellitus and hyperglycemia vary during the day with a patient's blood sugar. It is questionable whether this type of activity profile would lead one to assume that these agents would be useful for blood lipid control since Eng does not correlate the success of a treatment protocol or regimen for diabetes mellitus or hyperglycemia with success of the same treatment protocol or regimen in (1) lowering the levels of one or more serum lipids, (2)

reducing the serum LDL:HDL ratio, or (3) reducing the serum level of lipoprotein A (lp(A)) and/or apolipoprotein A (apo(A)) in a patient in need of each, as presently claimed.

The Examiner relied upon the secondary references, Raufman et al., J. Biol. Chem., 267:30, 21432-21437 (Oct. 1992) and Howard, Cur. Op. in Lipidology, 5:216-220 (1984), to explain that in Eng, "GLP-1(7-36) interacts with exendin receptors. See Raufman, page 21432, right column, last full paragraph." (first Office Action, p. 5) and that "[t]he cornerstone of therapy for diabetic patients [as in Eng] should essentially consider the management of dyslipidemia long with the hyperglycemia, hypertension, and obesity (Howard, page 219, left column)" (final Office Action, p. 3). However, this additional information does nothing to cure the deficiencies in Eng that are explained above.

Although the alleged interaction of GLP-1(7-36) with exendin receptors may be an interesting scientific hypothesis to explain the mechanism of the presently claimed invention, there is no disclosure in the prior art of using GLP-1(7-36) or an exendin with the intent of achieving the results in the present claims. This hindsight hypothesis does nothing to advance the Examiner's allegation of anticipation by Eng.

Next, the Examiner's belief that since "any and/or all patients, including diabetic and/or obese patients, including such patients with or without cardiovascular disease, are in need if such treatment because such treatment lowers the risk of cardiovascular disease in accordance with the present specification at page 2, full paragraph 2" (final Office Action, p. 4) adds nothing to Eng's disclosure since the presently pending claims do not call for the treatment of cardiovascular disease. Rather, they call for administering GLP-1 (7-37), GLP-1 (7-36) amide, exendin-3, exendin-4, or an

analogue or derivative of the foregoing with the intent of (1) lowering the levels of one or more serum lipids, (2) reducing the serum LDL:HDL ration, or (3) reducing the serum level of lipoprotein A (lp(A)) and 'or apolipoprotein A (apo(A)) in a patient respectively in need of each.

Howard's disclosure that those with diabetes mellitus or hyppoglycemia may also have cardiovascular disease does not show that Eng discloses administering GLP-1 (7-37), GLP-1 (7-36) amide, exendin-3, exendin-4, or an analogue or derivative of the foregoing with the intent of (1) lowering the levels of one or more serum lipids, (2) reducing the serum LDL:HDL ration, or (3) reducing the serum level of lipoprotein A (lp(A)) and 'or apolipoprotein A (apo(A)) in a patient respectively in need of each, either.

Howard states that "[a]gents which improve glycemic control sometimes also result in improvements in diabetic dyslipedemia." Howard, p. 218, right column. However, this is not a disclosure alone or in combination of Eng of specifically using GLP-1 (7-37), GLP-1 (7-36) amide, exendin-3, exendin-4, or an analogue or derivative of the foregoing with the intent of achieving the results presently claimed, either.

There is no express anticipation by Eng of any method presently claimed. There is no inherent anticipation by Eng either as there is no inherent intention of (1) lowering the levels of one or more serum lipids, (2) reducing the serum LDL:HDL ratio, or (3) reducing the serum level of lipoprotein A (lp(A)) and 'or apolipoprotein A (apo(A)) in a patient respectively in need of each. Eng does not anticipate claims 26-29, 36-42, 44-46, 48, 49, 51, 52, 54-56, 58, 59, 61, 62, 64-66, 68, 69, 71, and 72 in light of Raufman and/or Howard.

The second primary reference relied upon by the Examiner is Efendic et al., U.S. Patent No. 5,631,224. However, Efendic et al. discloses only the use of GLP-1 related peptides in combination with oral hypoglycemics to treat type 2 diabetes. col. 2, l. 65-col. 3, l. 4. Again, there is no disclosure of administering anything with the intent of (1) lowering the levels of one or more serum lipids, (2) reducing the serum LDL:HDL ratio, or (3) reducing the serum level of lipoprotein A (lp(A)) and/or apolipoprotein A (apo(A)) in a patient in need of each, as presently claimed. Consequently, Efendic et al. cannot anticipate pending claims 26, 27, 29, 36, 37, 39, 40, 42-46, 48, 49, 52, 54-56, 58, 59, 62-66, 68, 69, and 72.

The Examiner, with respect to Efendic et al., contends that since the present claims require administering a GLP-1 agonist to a patient in need of lowering the levels of one or more serum lipids, reducing the serum LDL:HDL ratio, or reducing the serum level of lipoprotein A (lp(A)) and/or apolipoprotein A (apo(A)), the only issue that must be considered for anticipation is "whether such a patient [in the prior art] knows that he is in need of such lowering or reduction." Advisory Action, p. 2, third paragraph. The Examiner is mistaken; he has misconstrued the present claims. The issue is not as he has stated; the issue is whether any prior art discloses administering anything with the intent of (1) lowering the levels of one or more serum lipids, (2) reducing the serum LDL:HDL ratio, or (3) reducing the serum level of lipoprotein A (lp(A)) and/or apolipoprotein A (apo(A)) in a patient in need of each. That is what the claims call for, and that is what the prior art must disclose in order to anticipate these claims. Knowledge is not intent in this context. The Examiner is wrong. Howard does not make Efendic et al. an anticipating reference either, just as it did not make Eng an anticipating reference. There is no express anticipation by

Efendic et al. of any method presently claimed. There is no inherent anticipation by Efendic et al. either as there is no inherent intention of (1) lowering the levels of one or more serum lipids, (2) reducing the serum LDL:HDL ratio, or (3) reducing the serum level of lipoprotein A (lp(A)) and/or apolipoprotein A (apo(A)) in a patient respectively in need of each. Efendic et al. does not anticipate claims 26, 27, 29, 36, 37, 39, 40, 42-46, 48, 49, 52, 54-56, 58, 59, 62-66, 68, 69, and 72 in light of Howard.

The above analyses are similar to those of the Court of Appeals for the Federal Circuit in *Rapoport v. Dement*, 254 F.3d 1053, 59 U.S.P.Q.2d 1215 (Fed. Cir. 2001). *Rapoport* was an appeal of this Board's denial of a motion that certain claims corresponding to an interference count were anticipated. The *Rapoport* count, in pertinent part, read:

> A method for treatment of sleep apneas comprising administration of a therapeutically effective amount of a Formula I azapirone compound or a pharmaceutically effective acid addition slat thereof to a patient in need of such treatment ....

The *Rapoport* court first construed the disputed term "treatment of sleep apneas" as a claim limitation having its plain and ordinary meaning, *i.e.*, performing the stated, which is treating sleep apneas, not treating symptoms commonly associated with the disorder but also present in patients without the disorder. *Rapoport*, 254 F.3d at 1059-60, 59 U.S.P.Q.2d at 1219-1220. Next, the court applied the prior art. The prior art disclosed the treatment of anxiety with the drug, buspirone, and that this drug had potential for treating patients having general breathing difficulties, including those with sleep apnea. However, the disclosed administration of the drug to those having sleep apnea was only with the intent of treating the anxiety symptom, not for intentionally treating the sleep apnea itself. The court found that there was no disclosure in the prior art "in which buspirone is

administered to patients suffering from sleep apnea with the intent to cure the underlying condition [i.e., the sleep apnea]." *Rapoport*, 254 F.3d at 1061, 59 U.S.P.Q.2d at 1220. Appellant Rapoport argued that "neither the reasons for administering buspirone to the patient nor the time of administration are relevant. Instead, according to [appellant] Rapoport, the only requirement of the count is that the patient suffer from sleep apnea." *Rapoport*, 254 F.3d at 1061, 59 U.S.P.Q.2d at 1221. The court held that given the proper claim construction, the prior art did not anticipate or render obvious the count.

Here, the prior art discloses treating diabetes mellitus. Just as in *Rapoport*, there is no prior art that is relied upon by the Examiner in the present appeal that discloses administering something to patients with the specific intent of (1) lowering the levels of one or more serum lipids, (2) reducing serum LDL:HDL ratio, or (3) reducing the serum level of lipoprotein A (lp(A)) and/or apolipoprotein A (apo(A)). The fact that some of the patients in Eng or Efendic et al. may have needed (1) lowering of the levels of one or more serum lipids, (2) reducing of the serum LDL:HDL ratio, or (3) reducing of the serum level of lipoprotein A (lp(A)) and/or apolipoprotein A (apo(A)) does not make either reference anticipating. Just as in *Rapoport*, the prior art relied upon by the Examiner here cannot anticipate any of the present claims.

B. Grounds of Rejection 3 and 4

The Examiner contends that pending claims 26-29 and 36-72 cannot be enabled for lowering one or more serum lipids, reducing the serum LDL:HDL ratio, and reducing the serum level of lp(A) or apo(A) because a study in 1996 did not observe an effect on levels of LDL or HDL after GLP-1 administration. Advisory Action, p. 2, 4th paragraph. The Examiner uses the same

reasoning to reject these claims as lacking a written description of their full scope. Advisory Action, p. 2, 5th paragraph.

A patent must enable the invention to be practiced by those in the relevant technical fields. 35 U.S.C. §112. The enablement requirement is met when the specification teaches a person of ordinary skill in the art how to make and use the claimed invention, without resort to undue experimentation. *Amgen, Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 1212, 18 U.S.P.Q.2d 1016, 1026 (Fed. Cir. 1991). Enablement is not negated because some experimentation is necessary. *Amgen*, 927 F.2d at 1212, 18 U.S.P.Q.2d at 1026 . It is also not necessary that all claimed embodiments are operable or that the applicant has tested all of them. *Atlas Powder Co. v. E.I. duPont de Nemours & Co*, 750 F.2d, 1569, 1576, 224 U.S.P.Q.2d, 409, 414 (Fed. Cir. 1984).

Furthermore, there is no reason to doubt the objective truth of statements in a patent application specification. *Fiers v. Revel*, 984 F.2d 1164, 1171-1172, 25 U.S.P.Q.2d 1601, 1607 (Fed. Cir. 1993). It is the Examiner's burden to provide a reasonable explanation of why the specification does not enable the scope of the pending claims. *In re Wright*, 999 F.2d 1557, 1561-1562, 27 U.S.P.Q.2d 510, 1513 (Fed. Cir. 1993). The Examiner has not carried his burden in the present appeal.

The only evidence presented by the Examiner to support these rejections is Juntti-Berggren, Diabetes Care, Vol. 19, No. 11, pp. 1200-1206 (Nov. 1996). The Examiner contends that this article shows that "[n]o changes were observed in the levels of LDL and HDL cholesterol after administration of GLP-1." Advisory Action, p. 2, 5th paragraph.

Juntti-Berggren reports a 14 day study of 12 patients. Four were given insulin only for 14 days, and eight were given insulin only for seven days, followed by insulin and GLP-1 for the next seven days.

This article is not relevant to the presently pending claims for the following reasons.

First, the protocol in the Juntti-Berggren study is only a single protocol in which GLP-1 was tested on only eight subjects. No information is given about their complete medical history, physical condition, activity, or regular diet. There was no routine optimization of dosage for the purpose of (1) lowering of the levels of one or more serum lipids, (2) reducing of the serum LDL:HDL ratio, or (3) reducing of the serum level of lipoprotein A (lp(A)) and/or apolipoprotein A (apo(A)). The present specification explains that, "[t]he particular GLP-1 agonist to be used and the optimal dose level for any patient (effective amount) will depend on the disease to be treated and on a variety of factors including the efficacy of the specific peptide derivative employed, the age, body weight, physical activity, and diet of the patient, on a possible combination with other drugs, and on the severity of the case. It is recommended that the dosage of the GLP-1 agonist be determined for each individual patient by those skilled in the art." Specification, p. 43, ll. 1-7. This is routine in the medical arts, but was not done in the Juntti-Berggren study. Consequently, the results of the Juntti-Berggren study are not indicative of anything with respect to the present claims.

Second, the standard deviations in the LDL and HDL levels in Table 4 of the article make the data suspect with respect to any findings concerning these figures.

Plainly, the Juntti-Berggren study does not give any reason to doubt the objective truth of statements in the present patent application specification, and the enablement rejection should be reversed.

A patent must also adequately describe the claimed invention. 35 U.S.C. §112. The description requirement is met when the patent specification conveys with reasonable clarity to those skilled in the art, as of the filing date of the application, that the inventor was in possession of the full scope of the invention, as claimed. The Examiner bears the burden of proving why persons of ordinary skill in the art would not recognize in the disclosure a description of the invention described in the claims. *In re Gosteli*, 872 F.2d 1008, 1112, 10 U.S.P.Q.2d 1614, 1618 (Fed. Cir. 1989).

Again, the present Examiner has failed to meet his burden here. In addition to the reasons discussed above, there is *ipsis verbis* support in the present specification for the pending claims. *See e.g.*, Specification, p. 1, l. 2; p. 3, ll. 4-5, 14-15; p. 5, ll. 7-8; p. 6, ll. 3-8.

The Examiner's rejection of the pending claims as lacking a written description should be reversed, as well.

C. Grounds of Rejection 5 and 8

The Examiner also contends that pending claims 26, 27, 29, 36, 37, 39, 40, 42, 44-49, 52, 54-59, 62, 64-69, and 72 are not supported by a written description of the full scope of the pending claims, *i.e.*, "'analogue' or 'derivative,' 'derivative of an analogue,' or 'exendin-4 analogue'" (final Office Action, p. 7) and that claims 44-49, 52, 54-59, 62, 64-69, and 72 are indefinite because of these terms.

The Examiner is incorrect on both issues because the present specification provides numerous examples of such compounds, these terms are well known in the art, and these terms have been accepted by the U.S. Patent and Trademark Office ("USPTO") in other patents in this field.

Copious examples are provided in the present application at Specification, p. 12, l. 15-p. 39, l. 33. Evidence that these terms are well-known in the art and are accepted by the USPTO can be found in, for example, U.S. Patent Nos. 6,747,006, claims 1 and 7, col, 3, l. 66-col. 4, l. 31 (Exh. 1); 6,593,295, claim 2 (Exh. 2); 6,583,111, claims 1, 19, and 28, col. 3, l. 41-col. 4, l. 6 (Exh. 3); 6,569,832, claims 7 and 15, col. 29, ll. 3-7 (Exh. 4); 6,444,788, 3, col. 26, ll. 34-37 (Exh. 5); 6,358, 924, claims 1 and 2, col. 4, ll 1-28 (Exh. 6); 6,348,447, claims 1 and 2 (Exh. 7); 6,191,102, claims 1 and 12, col. 3, l. 40-col. 4, l. 5 (Exh. 8); 6,344,180, claims 1 and 18, col. 4, ll. 52-53, col. 4, l. 17 (Exh. 9); 6,284,725, claim 2, col. 7, ll. 6-7, 38-39 (Exh. 10).

This makes it abundantly clear that the present applicants, as of the filing date of their application, were in possession of the full scope of the invention, as claimed. The Examiner has not met his burden, and the rejection should be reversed.

D. Grounds of Rejection 6 and 7

The Examiner is incorrect that claims 26-29, 36-42, 44-50, 52, 54-60, 62, 64-70, and 72 should be rejected under the judicially created doctrine of obviousness-type double patenting over claims 39 and 40 of U.S. Patent No. 6, 268,343 in view of Howard, Cur. Op. in Lipidology, 5:216-220 (1984) and Efendic et al., U.S. Patent No. 5,631,224, and over claims 19 and 20 of U.S. Patent No. 6,458,924 in view of Howard and Efedic et al. These rejections are improper because, again, the Examiner has misunderstood what is presently claimed.

The doctrine of obviousness-type double patenting only prohibits a party from "obtaining an extension of the right to exclude through claims in a later patent that are not patentably distinct from claims in a commonly owned earlier patent". *Eli Lilly & Co. v. Barr Laboratories, Inc.,* 251 F.3d 955, 967, 58 U.S.P.Q.2d 1865, 1877 (Fed. Cir. 2001). The specification of the earlier patent may not be utilized as prior art. *In re Vogel*, 422 F.2d 438, 441, 164 U.S.P.Q. 619, 622 (C.C.P.A. 1970); *In re Braat*, 937 F.2d 589, 594 n.5, 19 U.S.P.Q.2d 1289, 1298 n.5 (Fed. Cir. 1991). "[A] double patenting of the obviousness type rejection is 'analogous to [a failure to meet] the non-obviousness requirement of 35 U.S.C. §103,' except that the patent principally underlying the double patenting rejection is not considered prior art." *In re Longi*, 759 F.2d, 885, 892 n.4, 225 U.S.P.Q., 645, 648 n.4 (Fed Cir., 1985) (citing *In re Braithwaite*, 379 F.2d 594, 600 n.4, 154 U.S.P.Q. 29, 34 n.4 (C.C.P.A. 1967)). Therefore, the analysis in an obviousness-type double patenting rejection parallels that for an obviousness determination. *Id.*

Here, every presently appealed claim includes a preamble that, *inter alia*, states the specific purpose of the claim, and every appealed claim's preamble is a limitation that requires "that the method be practiced with the intent to achieve the stated objective." *Jansen,* 342 F.3d at 1333, 68 U.S.P.Q.2d at 1157-1158. However, claim 39 of U.S. Patent No. 6,268,343 claims "A method of treating diabetes, comprising administering to a patient a therapeutically effective amount of a GLP-1 derivative of claim 1," and claim 40 of this patent claims "A method of treating obesity, comprising administering to a patient a therapeutically effective amount of a GLP-1 derivative of claim 1." Claim 19 of U.S. Patent No. 6,458,924 claims "A method of treating diabetes, comprising administering to a patient a therapeutically effective amount of a GLP-1 derivative of claim 1," and

claim 20 of this patent claims "A method of treating obesity, comprising administering to a patient a therapeutically effective amount of a GLP-1 derivative of claim 1." Howard and Efendic et al. are discussed above with respect to Issues 1 and 2.

These '343 and '924 patent claims do not expressly or inherently disclose the administration of GLP-1 (7-37), GLP-1 (7-36) amide, exendin-3, exendin-4, or an analogue or derivative of the foregoing with the intent of (1) lowering the levels of one or more serum lipids, (2) reducing the serum LDL:HDL ratio, or (3) reducing the serum level of lipoprotein A (lp(A)) and/or apolipoprotein A (apo(A)) in a patient in need of each, respectively.

The Examiner relies upon the secondary references, Howard and Efendic et al., to show that "[t]he treatment of obesity or diabetes, as claimed in the patents [sic, the '343 patent], clearly overlaps the treatment of dyslipidemia, as presently claimed, as evidenced by Howard and Efendic." Final Office Action, p. 10. The Examiner again contends that "[t]he issue then is whether such a patient knows that he is in need of such lowering or reduction." Advisory Action, p. 3.

This additional information does nothing to cure the deficiencies of the cited claims of the '343 and '924 patents. There still is no intent to achieve the results presently claimed.

Furthermore, the Examiner's framing of the essential issue is simply wrong. The issue is whether the combination relied upon by the Examiner discloses administering GLP-1 (7-37), GLP-1 (7-36) amide, exendin-3, exendin-4, or an analogue or derivative of the foregoing with the intent of (1) lowering the levels of one or more serum lipids, (2) reducing the serum LDL:HDL ratio, or (3) reducing the serum level of lipoprotein A (lp(A)) and/or apolipoprotein A (apo(A)) in a patient respectively in need of each. *See Rapoport v. Dement*, 254 F.3d 1053, 59 U.S.P.Q.2d 1215 (Fed.

Cir. 2001). A patient's knowledge of his condition is not a disclosure of an intent to treat any such condition, as presently claimed. Here, the art relied upon by the Examiner discloses treating diabetes mellitus or obesity. Just as in *Rapoport*, there is no art that is relied upon by the Examiner in the present appeal that discloses administering something to patients with the specific intent of (1) lowering the levels of one or more serum lipids, (2) reducing serum LDL:HDL ratio, or (3) reducing the serum level of lipoprotein A (lp(A)) and/or apolipoprotein A (apo(A)). The fact that some of the patients in the cited art may have needed (1) lowering of the levels of one or more serum lipids, (2) reducing of the serum LDL:HDL ratio, or (3) reducing of the serum level of lipoprotein A (lp(A)) and/or apolipoprotein A (apo(A)) is not a proper basis for any rejection.

Accordingly both obviousness-type double patenting rejections should be reversed.

F. Ground of Rejection 9

Finally, the Examiner is incorrect in rejecting claims 45, 49, 55, 59, 65, and 69 under 35 U.S.C. 112, second paragraph as indefinite "because it is unclear if the analog is GLP-1(7-37) with a single amino acid substitution or some wholly undefined compound comprising an amino acid that is different from an amino acid in the corresponding position of GLP-1(7-37)." Final Office Action. p. 11.

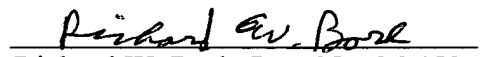
The rejection is confusing, but the plain language of the claims is clear. One amino acid residue of GLP-1(7-37) has been substituted by another. This is the GLP-1(7-37) analogue. This rejection should be reversed.

VIII. Conclusion

It is believed, for the foregoing reasons that all of the Examiner's rejections of the pending claims should be reversed.

Respectfully submitted,

Date: January 3, 2005



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APPENDIX OF CLAIMS

Claims 1-25 (Cancelled).

Claim 26 (Rejected) A method for lowering levels of one or more serum lipids in a patient, said method comprising administering to a patient in need of having one or more serum lipid levels lowered a lipid-lowering effective amount of a GLP-1 agonist, wherein said GLP-1 agonist is selected from the group consisting of GLP-1 (7-37), GLP-1 (7-36) amide, exendin-3, exendin-4, or an analogue or derivative of any of the foregoing.

Claim 27 (Rejected) The method according to claim 26, wherein said one or more serum lipids are selected from the group consisting of: low density lipoprotein (LDL); small, dense LDL; very low density lipoprotein (VLDL); triglycerides; free fatty acids; cholesterol; and high-density lipoprotein (HDL).

Claim 28 (Rejected) The method according to claim 26, wherein said GLP-1 agonist is selected from the group consisting of Arg^{26}, Lys^{34}(N-ε-(γ-Glu(N-α-hexadecanoyl)))-GLP-1(7-37), Arg^{34}, Lys^{26}(N-ε-(γ-Glu(N-α-hexadecanoyl)))-GLP-1(7-37), exendin-3, exendin-4, Val^{8}-GLP-1(7-37), Thr^{8}- GLP-1(7-37), Met^{8}- GLP-1(7-37), and Gly^{8}-GLP-1(7-37).

Claim 29 (Rejected) The method according to claim 26, wherein said GLP-1 agonist binds to a GLP-1 receptor with an affinity constant (Kd) below 1 μM.

Claims 30-35 (Cancelled).

Claim 36 (Rejected) The method according to claim 26, wherein said patient suffers from a disease state that is alleviated by lowering serum levels of said one or more lipids.

Claim 37 (Rejected) A method for reducing the serum LDL:HDL ratio in a patient, said method comprising administering to a patient in need of reduction of said LDL:HDL ratio a GLP-1 agonist in an amount effective to reduce said LDL:HDL ratio, wherein said GLP-1 agonist is selected from the group consisting of GLP-1 (7-37), GLP-1 (7-36) amide, exendin-3, exendin-4, or an analogue or derivative of any of the foregoing.

Claim 38 (Rejected) The method according to claim 37, wherein said GLP-1 agonist is selected from the group consisting of Arg^{26}, Lys^{34}(N-ε-(γ-Glu(N-α-hexadecanoyl)))-GLP-1(7-37), Arg^{34}, Lys^{26}(N-ε-(γ-Glu(N-α-hexadecanoyl)))-GLP-1(7-37), exendin-3, exendin-4, Val^{8}-GLP-1(7-37), Thr^{8}- GLP-1(7-37), Met^{8}- GLP-1(7-37), and Gly^{8}-GLP-1(7-37).

Claim 39 (Rejected) The method according to claim 37, wherein said GLP-1 agonist binds to a GLP-1 receptor with an affinity constant (Kd) below 1 μM.

Claim 40 (Rejected) A method for reducing the serum level of lipoprotein A (lp(A)) and/or apolipoprotein A (apo(A)) in a patient, said method comprising administering to a patient in need of reduction of the serum level of lipoprotein A (lp(A)) and/or apolipoprotein A (apo(A)) a GLP-1 agonist in an amount effective to reduce said serum level of lipoprotein A (lp(A)) and/or apolipoprotein A (apo(A)), wherein said GLP-1 agonist is selected from the group consisting of GLP-1 (7-37), GLP-1 (7-36) amide, exendin-3, exendin-4, or an analogue or derivative of any of the foregoing.

Claim 41 (Rejected) The method according to claim 40, wherein said GLP-1 agonist is selected from the group consisting of Arg^{26}, Lys^{34}(N-ε-(γ-Glu(N-α-hexadecanoyl)))-GLP-1(7-37), Arg^{34}, Lys^{26}(N-ε-(γ-Glu(N-α-hexadecanoyl)))-GLP-1(7-37), exendin-3, exendin-4, Val^{8}-GLP-1(7-37), Thr^{8}- GLP-1(7-37), Met^{8}- GLP-1(7-37), and Gly^{8}-GLP-1(7-37).

Claim 42 (Rejected) The method according to claim 40, wherein said GLP-1 agonist binds to a GLP-1 receptor with an affinity constant (Kd) below 1 μM.

Claim 43 (Rejected) The method according to claim 26, wherein the GLP-1 agonist is GLP-1 (7-37) or GLP-1 (7-36) amide.

Claim 44 (Rejected) The method according to claim 26, wherein the GLP-1 agonist is an analogue of GLP-1 (7-37).

Claim 45 (Rejected) The method according to claim 44, wherein in the analogue of GLP-1 (7-37), one amino acid residue of GLP-1 (7-37) has been substituted by another amino acid residue.

Claim 46 (Rejected) The method according to claim 26, wherein the GLP-1 agonist is a derivative of GLP-1 (7-37).

Claim 47 (Rejected) The method according to claim 46, wherein the derivative of GLP-1 (7-37) has one or more lipophilic substituents.

Claim 48 (Rejected) The method according to claim 46, wherein the derivative of GLP-1 (7-37) is a derivative of an analogue of GLP-1 (7-37).

Claim 49 (Rejected) The method according to claim 48, wherein in the analogue of GLP-1 (7-37), one amino acid residue of GLP-1 (7-37) has been substituted by another amino acid residue.

Claim 50 (Rejected) The method according to claim 49, wherein the derivative is Arg^{34}, Lys^{26}(N-ε-(γ-Glu(N-α-hexadecanoyl)))-GLP-1(7-37).

Claim 51 (Rejected) The method according to claim 26, wherein said GLP-1 agonist is exendin-4

Claim 52 (Rejected) The method according to claim 26, wherein said GLP-1 agonist is an exendin-4 analogue.

Claim 53 (Rejected) The method according to claim 37, wherein the GLP-1 agonist is GLP-1 (7-37) or GLP-1 (7-36) amide.

Claim 54 (Rejected) The method according to claim 37, wherein the GLP-1 agonist is an analogue of GLP-1 (7-37).

Claim 55 (Rejected) The method according to claim 54, wherein in the analogue of GLP-1 (7-37), one amino acid residue of GLP-1 (7-37) has been substituted by another amino acid residue.

Claim 56 (Rejected) The method according to claim 37, wherein the GLP-1 agonist is a derivative of GLP-1 (7-37).

Claim 57 (Rejected) The method according to claim 56, wherein the derivative of GLP-1 (7-37) has one or more lipophilic substituents.

Claim 58 (Rejected) The method according to claim 56, wherein the derivative of GLP-1 (7-37) is a derivative of an analogue of GLP-1 (7-37).

Claim 59 (Rejected) The method according to claim 58, wherein in the analogue of GLP-1 (7-37), one amino acid residue of GLP-1 (7-37) has been substituted by another amino acid residue.

Claim 60 (Rejected) The method according to claim 59, wherein the derivative is Arg^{34}, Lys^{26}(N-ε-(γ-Glu(N-α-hexadecanoyl)))-GLP-1(7-37).

Claim 61 (Rejected) The method according to claim 37, wherein said GLP-1 agonist is exendin-4

Claim 62 (Rejected) The method according to claim 37, wherein said GLP-1 agonist is an exendin-4 analogue.

Claim 63 (Rejected) The method according to claim 40, wherein the GLP-1 agonist is GLP-1 (7-37) or GLP-1 (7-36) amide.

Claim 64 (Rejected) The method according to claim 40, wherein the GLP-1 agonist is an analogue of GLP-1 (7-37).

Claim 65 (Rejected) The method according to claim 64, wherein in the analogue of GLP-1 (7-37), one amino acid residue of GLP-1 (7-37) has been substituted by another amino acid residue.

Claim 66 (Rejected) The method according to claim 40, wherein the GLP-1 agonist is a derivative of GLP-1 (7-37).

Claim 67 (Rejected) The method according to claim 66, wherein the derivative of GLP-1 (7-37) has one or more lipophilic substituents.

Claim 68 (Rejected) The method according to claim 66, wherein the derivative of GLP-1 (7-37) is a derivative of an analogue of GLP-1 (7-37).

Claim 69 (Rejected) The method according to claim 68, wherein in the analogue of GLP-1 (7-37), one amino acid residue of GLP-1 (7-37) has been substituted by another amino acid residue.

Claim 70 (Rejected) The method according to claim 69, wherein the derivative is Arg^{34}, Lys^{26}(N-ε-(γ-Glu(N-α-hexadecanoyl)))-GLP-1(7-37).

Claim 71 (Rejected) The method according to claim 40, wherein said GLP-1 agonist is exendin-4

Claim 72 (Rejected) The method according to claim 40, wherein said GLP-1 agonist is an exendin-4 analogue.